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TITLE: Nasal Irrigation for Chronic Rhinosinusitis and Fatigue in Patients with Gulf War Syndrome

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14. ABSTRACT The purpose of this research effort is to conduct a randomized controlled trial (RCT): "Nasal Irrigation for Chronic Rhinosinusitis and Fatigue in Patients with Gulf War Illness" which will evaluate the effects of two different types of nasal irrigation solution compared to a control group for sinus and fatigue symptoms in adults with GWI. The primary activities conducted during year three of the project involved continued coordination with the Madison Veterans Affairs Hospital (VA) for subject identification and recruitment, and subject recruitment and enrollment.					
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INTRODUCTION

More than 50,000 troops returned from the Persian Gulf conflicts reporting a myriad of medically unexplained symptoms with no identifiable etiology. While patients who meet the case definition of Gulf War Illness (GWI) can have a myriad of symptoms, two of the most prevalent and debilitating ones are chronic nasal congestion and fatigue. The purpose of this research effort is to conduct a randomized controlled trial (RCT): “Nasal Irrigation for Chronic Rhinosinusitis and Fatigue in Patients with Gulf War Illness” which will evaluate the effects of two different types of nasal irrigation solution compared to a control group for sinus and fatigue symptoms in adults with GWI.

BODY

The major objectives of the study are twofold: 1) To find an effective adjunctive therapy for veterans with Gulf War Illness (GWI) and symptoms of chronic rhinosinusitis (CRS) and fatigue and 2) To evaluate the proinflammatory bias of each individual’s profile at baseline and in response to therapy. Statistically positive results on clinical outcome measures would demonstrate that nasal irrigation (NI) can provide effective adjunctive therapy for CRS and fatigue, improving quality of life for GWI-affected patients and potentially to society through reduced use of medical resources and absenteeism. Positive findings on cytokine and cellular assessment would shed light on the etiology of CRS and fatigue in the GWI population and contribute to the understanding of each; positive response to therapy would elucidate a biological mechanism of action of NI. Finally, the finding that NI, adjunctive to routine care, is more cost effective than “routine care only” would provide economic justification for its clinical use in the studied population.

The primary activities conducted during year three of the project involved the enrollment, retention, coordination and management of study subjects and data collection. Currently, the study has enrolled 24 subjects, 4 of whom have completed the study. There are 7 subjects who have passed the telephone screen and are potentially eligible; these potential participants have been scheduled for secondary screen and if eligible, will be scheduled for enrollment in the upcoming weeks.

Data entry and management via the secure study database is ongoing. The updated subject database has been invaluable in tracking enrolled subjects.

The study mechanics are functioning well; randomization is producing 3 comparable groups; all data acquisition is going well with high data capture rates.

The study design for initial subject identification primarily uses an ICD-9 code screen to identify veterans who were in the first Gulf War and with the appropriate diagnoses for chronic rhinosinusitis or fatigue in the past two years [CRS (473.*) or fatigue (780.7)]. As potential subjects are identified, we conduct outreach through mailings and have obtained approval from the UW Health Sciences IRB for an expanded protocol. The protocol included community recruitment methods such as tear-off flyers in public places veterans might frequent, presentations of study information to VFW and other veterans groups and electronic informational advertisements to be posted on VFW websites and listservs. These recruitment methods are designed to identify veterans who receive care outside the VA system. We also

plan to expand this pool of additional potential subjects by screening the billing ICD-9 databases of other VA hospitals in the VISN-12 network (VA Great Lakes Health Care System). We plan to expand this pool of additional potential subjects by screening the billing ICD-9 databases of other VA hospitals in the VISN-12 network (VA Great Lakes Health Care System). This will provide us with access to Gulf War Veterans living in Milwaukee, WI; Chicago, IL, and surrounding areas. A request has been made to the office of the Chief of Staff of the Madison VA Hospital for expansion of recruitment to the VISN-12 network.

The study also obtained continuing approvals from the UW Institutional Review Board, the VA Research Committee and the USAMRMC/Human Research Protections Office.

The manufacturer (Danisco/Dupont) of xylitol has continued to provide daily use packets at no cost as indicated in the protocol and letter of support in the initial grant application.

The table below is a summary of eligible and/or enrolled subjects recruited from the VA and the community during the reporting period.

	VA Recruitment	Community Recruitment	Total
Eligible subjects	32	5	37
Enrolled subjects	21	3	24

As study activities progress, study team members will continue to meet with staff associated with the UW Clinical Research Unit (CRU) to review clinical services to be utilized by the study as well as the Pharmaceutical Research Center (PRC) which will be housing and dispensing all study medications (Xylitol and Saline). We have final approval on all procedures associated with these two entities and continue to enroll and schedule subjects.

The study recently underwent a random/routine institutional audit by the University of Wisconsin Institute of Clinical and Translational Research. The audit was completed with very positive feedback and minor suggestions were made for maximizing study quality.

The study team has also been in transition with the recent hiring of a new study coordinator. The change in study personnel has not hampered project activities and enrollment has continued as projected.

The project recently submitted a request for a no cost extension of the grant award. This application was warranted due to the unexpected length of time for study approval processes conducted in year 1 of the study. The project anticipates receiving approval of this submission and will continue with planned study activities.

KEY RESEARCH ACCOMPLISHMENTS:

- Study approval from all relevant stakeholders (UW HS IRB, VA R & D Committee, DHSC)
- Expansion of recruitment strategies
- Procurement of xylitol
- Recruitment and enrollment of subjects

REPORTABLE OUTCOMES:

- UW HS IRB continuing review study approval
- VA R & D Committee continuing review study approval
- Refinement of study tracking database

Upcoming activities planned for the project include:

- Regional expansion of subject identification and recruitment
- Completion of subject recruitment and enrollment
- Continued subject follow up
- Preliminary data analysis

CONCLUSION: As stated, the purpose of this research effort is to evaluate the effects of two different types of nasal irrigation solution compared to a control group for sinus and fatigue symptoms in adults with GWI. While there have been inevitable practical and administrative hurdles, and the study team is new to research work within Veterans Administration structures, the study has continued enrollment and collection of high quality data. General success for either form of NI compared to routine care would provide an immediately accessible treatment to improve the quality of life of veterans with GWI, CRS and fatigue. Because of the likely overlap between the underlying etiologies of CRS and fatigue between GWI vets and the general population, success may also translate to a more general population. Positive findings would suggest a number of important effects:

- Statistically positive results on HRQoL outcome measures would suggest that NI can provide effective adjunctive therapy for CRS and fatigue in adults with GWI, improving health of affected patients and potentially providing gains to society through reduced health care utilization and absenteeism related costs.
- Positive biomarker findings would contribute to our better understanding of the etiology of CRS and fatigue in the GWI population and of possible biological pathways underlying the NI efficacy.
- The finding that either form of NI is cost effective would provide economic justification for its clinical use.

REFERENCES: NA

APPENDICES:

Attachment A: UW HS IRB Continuing Review approval – VA protocol

Attachment B: UW HS IRB Continuing Review approval – community protocol

Attachment C: VA R&D Committee Continuing Review approval



Health Sciences IRB

4/30/2014

Submission ID number: [2011-0843-CR002](#)

Title: Nasal Irrigation for Chronic Rhinosinusitis and Fatigue in Patients with Gulf War Illness(GW100054)

Principal Investigator: DEAN D KRAHN

Point-of-contact: DIANA L MYERS

IRB Staff Reviewer: MOLLY LUMLEY

The convened HS IRB conducted a full review of the above-referenced continuing review progress report. The study was approved for the period of 12 months with the expiration date of 4/28/2015.

To access the materials approved by the IRB, including any stamped consent forms and recruitment materials, please log in to your ARROW account and view the documents tab in the submission's workspace.

Please review the Investigator Responsibilities guidance (<http://go.wisc.edu/m0lovn>), which includes a description of IRB requirements for submitting continuing review progress reports, changes of protocol and reportable events.

Please contact the appropriate IRB office with general questions: Health Sciences IRBs at 608-263-2362 or Education and Social/Behavioral Science IRB at 608-263-2320. For questions related to this submission, contact the assigned staff reviewer.



Health Sciences IRB

4/23/2014

Submission ID number: [2012-1126-CR001](#)

Title: Nasal Irrigation for Chronic Rhinosinusitis and Fatigue in Patients with Gulf War Illness - Community Recruitment

Principal Investigator: DAVID RABAGO

Point-of-contact: JESSICA GRETTIE

IRB Staff Reviewer: JESSICA JOHNSON

A designated HS IRB member conducted an expedited review of the above-referenced continuing review progress report form. The study was approved by the IRB member for the period of 12 months with the expiration date of 4/22/2015. The study qualified for expedited review pursuant to 45 CFR 46.110 and, if applicable, 21 CFR 56.110 and 38 CFR 16.110:

Category 8: The study was previously approved by the convened IRB and no subjects have been enrolled and no additional risks have been identified

To access the materials approved by the IRB, including any stamped consent forms and recruitment materials, please log in to your ARROW account and view the documents tab in the submission's workspace.

Please review the Investigator Responsibilities guidance (<http://go.wisc.edu/m0lovn>), which includes a description of IRB requirements for submitting continuing review progress reports, changes of protocol and reportable events.

Please contact the appropriate IRB office with general questions: Health Sciences IRBs at 608-263-2362 or Education and Social/Behavioral Science IRB at 608-263-2320. For questions related to this submission, contact the assigned staff reviewer.

**Department of
Veterans Affairs**

Memorandum

Date: May 12, 2014
From: Associate Chief of Staff for Research
Subj: Continuing Review
To: Dr. Dean Krahn
Dr. David Rabago

The continuing review report for your study entitled "Nasal Irrigation for Chronic Rhinosinusitis and Fatigue in Patients with Gulf War Illness (GW100054)" (UW HS IRB #2011-0843, CR002), as reviewed and approved by the IRB, has been reported to and accepted by the R&D Committee on May 6, 2014. This study is now approved as meeting VA continuing review requirements until the expiration date specified on the IRB notice.

A handwritten signature in blue ink, appearing to read 'Nas', with a stylized flourish extending to the right.

NASIA SAFDAR, MD, PhD